



Express Mail No.: EV 475 142 079 US

Doc Code: AP.PRE.REQ

PTO/SB/33 (07-05)

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## PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)

8932-296-999

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on \_\_\_\_\_

Signature \_\_\_\_\_

Typed or printed name \_\_\_\_\_

Application Number

09/769,404

Filed

January 26, 2001

First Named Inventor

Wallimann et al.

Art Unit

1617

Examiner

Shengjun Wang

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).

Note: No more than five (5) pages may be provided.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.  
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.  
(Form PTO/SB/96)

☒ attorney or agent of record.  
Registration number 49,013

☐ attorney or agent acting under 37 CFR 1.34.

Registration number if acting under 37 CFR 1.34 \_\_\_\_\_

Ann W. Chen

Signature

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Typed or printed name

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Telephone number

January 20, 2006

Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below\*.

☒ \*Total of 1 forms are submitted.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 8932-296-999

Group Art Unit: 1617 )  
)  
Examiner: Shengjun Wang )  
)  
Inventor: Wallimann et al. )  
)  
Serial No.: 09/769,404 )  
)  
Filed: January 26, 2001 )  
)  
For: METHODS OF TREATING )  
BONE OR CARTILAGE )  
CONDITIONS BY THE )  
ADMINISTRATION OF )  
CREATINE )

**PRE-APPEAL BRIEF  
CONFERENCE REQUEST**

Mail Stop AF  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Applicants hereby request review of the Final Rejection mailed September 20, 2005 ("Final Rejection") of the above-captioned application prior to filing an appeal brief for the reasons set forth below. Applicants submit that the Final Rejection fails to establish a *prima facie* rejection.

**I. PROSECUTION SUMMARY**

Independent claims 1, 22-24 and 28 were rejected in a Non-Final Office Action mailed January 12, 2005 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,998,458 to Kaddurah-Daouk ("Kaddurah-Daouk") in view of U.S. Patent No. 4,772,591 to Meisner ("Meisner"), U.S. Patent No. 5,888,553 to Grant *et al.* ("Grant"), U.S. Patent No. 5,756,469 to Beale ("Beale '469"), and U.S. Patent No. 5,716,926 to Beale *et al.* ("Beale '926"). In response, Applicants:

- amended claim 1 to recite that the agent comprises “creatine pyruvate” and is “administered in an amount of 1.4 to 285 mg per day;”
- amended claims 23 and 24 to recite that the agent comprises “creatine pyruvate;” and
- cancelled claim 28.

In response, the Examiner finally rejected claims 1-3, 13-14 and 21-24 in the Final Rejection under 35 U.S.C. § 103(a) as being unpatentable over Kaddurah-Daouk in view of Meisner, Grant, Beale ‘469, and Beale ‘926. The Examiner stated that Kaddurah-Daouk does not teach expressly the employment of creatine pyruvate for the treatment, or the particular amount administered, or the method may be employed for promoting growth and mineralization of bone; improving acceptance and osseous integration of bone; or accelerating healing as claimed in claims 22-24, or the purity as herein required. The Examiner further state that (1) Kaddurah-Daouk teaches that creatine compounds are useful for treating osteoporosis or osteoarthritis; (2) Grant teaches that excess of cortisol is a cause of osteoporosis, tissue degeneration, and an anabolic composition comprising creatine has anticortisol effect that is useful for balancing the effect of cortisol; (3) Meisner teaches that creatine is useful for accelerating wound healing or for treating degenerative disorders including periodontal disease, osteoarthritis; (4) Beale ‘469 teaches that pyruvyl-creatine is particularly useful as a cortisol antagonist or cortisol blocker, and (5) Beale ‘926 teaches that pyruvate is known to be useful for treating osteoporosis. (Final Rejection at pp. 2-3). The Examiner thereafter stated that it was *prima facie* obvious to make the required combination to practice the claimed invention. (Final Rejection at p. 3). In addition, the Examiner stated that a *prima facie* case of obviousness exists with respect to claim 1 since the claimed dosage ranges overlap or lie inside ranges disclosed by the prior art. (Final Rejection at p. 5). Moreover, in regards to claims 22-24, the Examiner asserted that using creatine to promote growth and mineralization of bone (claim 22), improve acceptance and osseous integration of bone implants (claim 23), and accelerate healing in a subject having a defect in bone or

cartilage tissue caused by trauma or surgery (claim 24) are obvious since creatine is known to be useful for promoting tissue (cartilage) repair and treating osteoporosis, which is to promote mineralization of bone. (Final Rejection at p. 4).

## **II. FAILURE TO ESTABLISH A *PRIMA FACIE* CASE OF OBVIOUSNESS**

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, the prior art reference(s) must teach or suggest all the claim limitations. Second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Third, there must be a reasonable expectation of success. A *prima facie* case of obviousness has not been made with regard to independent claims 1 and 22-24 and their dependent claims for the following reasons:

First, the Examiner has failed to show that any one of the cited references disclose, teach or suggest the use of creatine pyruvate to treat a bone or cartilage defect, as recited in claim 1; to promote bone growth and mineralization, as recited in claim 22; to improve bone acceptance and osseous integration, as recited in claim 23; or to accelerate healing, as recited in claim 24. The Examiner admits that Kaddurah-Daouk fails to teach or suggest creatine pyruvate (see Final Rejection at p. 2, point no. 4). Meisner and Grant also fail to teach or suggest the use of creatine pyruvate. While Beale '469 mentions the use of the cortisol blocker ipriflavone to treat osteoporosis (see Beale '469, col. 3, lines 46-49), there is no teaching or suggestion in Beale '469 that creatine pyruvate can be used to treat osteoporosis. While Beale '926 discloses the treatment of osteoporosis by the administration of calcium pyruvate (see Beale '926, col. 5, lines 17-18), Beale '926 never identifies creatine pyruvate, much less teach or suggest the use of creatine pyruvate to treat a bone or cartilage defect, as recited in claim 1; to promote bone growth and mineralization, as recited in claim 22; to improve bone acceptance and osseous integration, as recited in claim 23; or to accelerate healing, as recited in claim 24.

In addition, none of the references, either alone or together, teach or suggest the ranged recited in claim 1. The claimed range does not overlap or lie inside ranges disclosed by the cited references. In fact, Kaddurah-Daouk, Beale '469, and Beale '926 teach administering pyruvate to subjects in amounts that are considerably higher than the upper end of the recited range (*i.e.*, 285 mg per day). For example, Kaddurah-Daouk discloses that creatine can be administered in an amount of 2 to 8 g per day (see Kaddurah-Daouk, col. 11, lines 29-31); Beale '469 discloses that "[i]n the method of the present invention, the mammal, preferably human, consumes at least 5 g per day of the pyruvate/cortisol blocker composition" (see Beale '469, col. 6, lines 8-10); and Beale '926 discloses administering the anabolic protein/pyruvate composition to a mammal in the amount of from 1 to 300 g per day (see Beale '926, col. 5, lines 26-28). As such, Kaddurah-Daouk, Beale '469, and Beale '926 all teach away from the significantly smaller amounts recited in claim 1, *i.e.*, 1.4 to 285 mgs per day or 0.0014 to 0.285 g per day.

Even if Kaddurah-Daouk, Meisner, Grant, Beale '469, and Beale '926, together, did disclose the use of creatine pyruvate to practice the claimed methods (which they do not), there is no suggestion or motivation in any of the references to modify the references or to combine the reference teachings in a manner to arrive at the invention of independent claim 1, 22, 23 or 24. Kaddurah-Daouk, Meisner, Grant, Beale '469, and Beale '926 relate to three different technical fields. Kaddurah-Daouk teaches a method of treating a metabolic disorder such as obesity or severe weight loss, Meisner teaches a method of healing wounds, and each of Grant, Beale '469, and Beale '926 teaches a method of increasing muscle mass. Applicants submit that one skilled in the art of metabolic disorder treatment would have no motivation to modify or combine the teaching of Kaddurah-Daouk with Meisner, Grant, Beale '469, and Beale '926. Likewise, one skilled in the art of wound healing would have no motivation to apply the teaching of Kaddurah-Daouk, Grant, Beale '469, or Beale '926 to Meisner. Nor would one skilled in the art of body building have motivation to modify or

combine the teachings of Grant, Beale '469, or Beale '926 with Kaddurah-Daouk and/or Meisner. Therefore, based on these cited references, one skilled in the art would have absolutely no motivation to combine the references, and certainly no motivation to combine the references in a manner to arrive at the claimed method of treatments provided in claim 1, 22, 23 or 24. Lastly, even if there was a modicum of motivation to combine the references, there is no motivation to combine the references with any reasonable expectation of arriving at the claimed invention.

Applicants submit that the Examiner has improperly used hindsight reconstruction to pick and choose among isolated disclosures in Kaddurah-Daouk, Meisner, Grant, Beale '469, and Beale '926 to reconstruct the claimed invention. The use of five disparate references from which to pick and choose isolated disclosures without regard to the reference as a whole is indicative of such hindsight reconstruction. In particular, Applicants respectfully submit that *hindsight reconstruction* has been used in the rejection of the present invention to combine a metabolic disorder treatment with a wound healing therapy and a body building regimen. Such hindsight, however, is improper and should be avoided in determining patentability.

### III. CONCLUSION

For at least the above reasons, Applicants submit that independent claims 1 and 22-24 are in condition for allowance. As claims 2-3,13-14 and 21 depend from independent claim 1, Applicants submit these claims are likewise in condition for allowance.

Respectfully submitted,

Date: January 20, 2006

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